TSEN54 gene

tRNA splicing endonuclease subunit 54

Normal Function

The *TSEN54* gene provides instructions for making one part (subunit) of an enzyme called the tRNA splicing endonuclease complex. This complex helps process several types of RNA molecules, which are chemical cousins of DNA.

The tRNA splicing endonuclease complex is particularly important for the normal processing of a form of RNA known as transfer RNA (tRNA). tRNA molecules help assemble protein building blocks called amino acids into full-length proteins. However, before they can assemble proteins, tRNAs must be processed into mature molecules. In particular, regions called introns need to be removed from some tRNAs for the molecules to be functional. The tRNA splicing endonuclease complex recognizes and then removes introns to help produce mature tRNA molecules.

Studies suggest that the tRNA splicing endonuclease complex may also be involved in processing another form of RNA known as messenger RNA (mRNA). mRNA serves as a genetic blueprint for making proteins. Researchers suspect that the tRNA splicing endonuclease complex cuts (cleaves) one end of mRNA molecules so a string of adenines (one of the building blocks of RNA) can be added. This process is known as polyadenylation, and the string of adenines is known as a poly(A) tail. The poly(A) tail signals the stopping point for protein production and protects mRNA from being broken down before protein production occurs.

Health Conditions Related to Genetic Changes

pontocerebellar hypoplasia

Several mutations in the *TSEN54* gene have been identified in people with a disorder of brain development called pontocerebellar hypoplasia. The major features of this condition include delayed development, problems with movement, and intellectual disability. *TSEN54* gene mutations are the most frequent cause of a form of the disorder designated pontocerebellar hypoplasia type 2 (PCH2). When PCH2 results from *TSEN54* gene mutations, it is sometimes categorized more specifically as PCH2A. Mutations in the *TSEN54* gene also cause pontocerebellar hypoplasia type 4 (PCH4) and appear to be a rare cause of pontocerebellar hypoplasia type 1 (PCH1).

The most common mutation in the *TSEN54* gene replaces the amino acid alanine with the amino acid serine at position 307 in the TSEN54 protein (written as Ala307Ser or A307S). About 90 percent of all people with PCH2 have this mutation in both copies of the *TSEN54* gene in each cell. At least one person diagnosed with

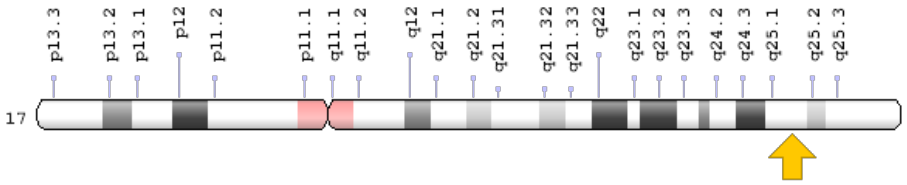
PCH1 also had the mutation in both copies of the gene. Most individuals with PCH4 have the common Ala307Ser mutation in one copy of the *TSEN54* gene in each cell and a different mutation in the other copy of the gene.

The *TSEN54* gene mutations that cause pontocerebellar hypoplasia impair the function of the tRNA splicing endonuclease complex, which likely disrupts the processing of RNA molecules and affects the production of many types of proteins. Before birth, these changes appear to have the most severe impact on fast-growing tissues, such as those in the brain. However, it is unknown exactly how reduced function of the tRNA splicing endonuclease complex leads to abnormal brain development in people with pontocerebellar hypoplasia.

Chromosomal Location

Cytogenetic Location: 17q25.1, which is the long (q) arm of chromosome 17 at position 25.1

Molecular Location: base pairs 75,516,528 to 75,524,739 on chromosome 17 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FLJ37147
- SEN54
- SEN54_HUMAN
- SEN54L
- tRNA-intron endonuclease Sen54
- tRNA splicing endonuclease 54 homolog
- tRNA splicing endonuclease 54 homolog (S. cerevisiae)
- TSEN54 tRNA splicing endonuclease subunit

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): From RNA to Protein
  https://www.ncbi.nlm.nih.gov/books/NBK26829/
- Molecular Biology of the Cell (fourth edition, 2002): Structure of a tRNA-splicing endonuclease docked to a precursor tRNA (figure)
  https://www.ncbi.nlm.nih.gov/books/NBK26829/?rendertype=figure&id=A1060
- The Cell: A Molecular Approach (second edition, 2000): Processing of mRNA in Eukaryotes
  https://www.ncbi.nlm.nih.gov/books/NBK9864/#A1031

GeneReviews

- TSEN54-Related Pontocerebellar Hypoplasia
  https://www.ncbi.nlm.nih.gov/books/NBK9673

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TSEN54%5BTIAB%5D%29+OR+%28tRNA+splicing+endonuclease%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- tRNA SPLICING ENDONUCLEASE 54, S. CEREVISIAE, HOMOLOG OF
  http://omim.org/entry/608755

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=TSEN54%5Bgene%5D
- HGNC Gene Family: tRNA-splicing endonuclease subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/776
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=27561
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/283989
- UniProt
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